Remarks

This is a response to the Office Action dated November 20, 2001, the period for response to which has been extended from February 20, 2002 to May 20, 2002.

In the Office Action, the Examiner (1) requests affirmation of the telephonic election of species, (2) rejects Claims 1-19 under 35 U.S.C. 112, first paragraph, (3) rejects Claims 3, 4, 8-10 and 14-18 under 35 U.S.C. 112, second paragraph, (4) rejects Claims 1 and 4-10 under 35 U.S.C. 102(e) and (5) rejects Claims 1, 4-7 and 9-10 under 35 U.S.C. 103.

In this response, Applicants traverse the rejections and respectfully request reconsideration and allowance of the claims.

The claims have been amended herein in response to the restriction requirement, to clarify the invention being claimed and to introduce new Claims 20-21. The amendments are fully supported by the specification as filed and they do not introduce new matter.

Lastly, Applicants submit herewith a Supplemental Information Disclosure Statement.

Supplemental Information Disclosure Statement

The following information is submitted pursuant to 37 C.F.R. 1.97 and 1.98 in accordance with Applicants' duty of disclosure under 37 C.F.R. 1.56. This submission is not an admission that the document cited herein is prior art as to the invention claimed. Because this Information Disclosure Statement is submitted after the first Office Action on the merits, but before the issuance of a final action or a notice of allowance, Applicants hereby expressly authorize the Commissioner to charge the appropriate fee of $180.00 (or other amount as required under 37 C.F.R. 1.17(p) to Deposit Account No. 01-0025. Duplicate copies of this sheet are enclosed. A Form PTO 1449 listing this reference is submitted herewith.

The following reference is know to the Applicants:

1. Hauer, et al., U.S. Patent No. 5,342,625, issued August 30, 1994.

Election of Species

Applicants affirm that in a telephone conference with the Examiner on November 6, 2001, Applicants' agent, Dr. Steven Crowley, elected the species ritonavir, with the understanding that the Examiner would examine any claims comprising ritonavir.

Section 112 Rejections

The Examiner rejects Claims 1-19 under 35 U.S.C.112, first paragraph. The Examiner questions the efficacy of the HIV protease inhibitor compositions. Applicants assert that ritonavir is a well-known HIV protease inhibitor and that ritonavir has been approved as a safe and efficacious HIV therapeutic agent throughout the world, usually under the tradename of NORVIR.

Therefore, Applicants respectfully request that the Examiner reconsider and withdraw the Section 112, first paragraph, rejection.

The Examiner also rejects Claims 3, 4, 8-10 and 14-18 under 35 U.S.C. 112, second paragraph, as being indefinite. Applicants disagree that these claims are indefintie. Nonetheless, the amendments submitted herein address the issues raised by the Examiner regarding Claims 3, 4 and 10.

Regarding Claims 8-9 and 14-18, Applicants assert that the claims use the phrase "comprising". Therefore, the indicated components are present, but other components may also be present. As a result, the amounts of the indicated components, when totaled, may or may not make up 100% of the total solution.

In view of the above, Applicants respectfully request that the Examiner reconsider and withdraw the Section 112, second paragraph, rejection.

Section 102 Rejection

The Examiner rejects Claims 1 and 4-10 under 35 U.S.C. 102(e) as being anticipated by Al-Razzak, et al., U.S. Patent No. 5,948,436. Applicants assert that the Al-Razzak reference does not disclose or suggest the presently claimed composition. In particular, the Al-Razzak reference does not disclose or suggest a composition in which the solvent comprises a medium and/or long chain fatty acid. Therefore, the Examiner is respectfully requested to reconsider and withdraw the Section 102 rejection.

Section 103 Rejections

The Examiner rejects Claims 1, 4-7 and 9-10 under 35 U.S.C. 103 as being unpatentable over Sham, et al., International Patent Application WO97/21685. The Examiner also rejects Claims 1, 4-7 and 9-10 under 35 U.S.C. 103 as being unpatentable over Sham, et al., U.S. Patent No. 5,914,332. Applicants assert that the disclosures of both references are the same. Applicants assert that neither reference teaches or suggests the claimed invention. In particular, Applicants assert that neither reference discloses or suggests including water in the solution of ritonavir. In addition, Applicants assert that neither reference discloses or suggests that the addition of water to the solution of ritonavir will provide enhanced solubility of ritonavir in the solution.

Therefore, the Examiner is respectfully requested to reconsider and withdraw the Section 103 rejections.

Action Requested

In view of the above, reconsideration and allowance of Claims 1, 3-11 and 14-19 (as amended) and new Claims 20-21 is respectfully requested.

Respectfully submitted,
L. Alani, et al.

Dr. Steven R. Crowley
Registration No. 31,604
Agent for Applicants

23492

ABBOTT LABORATORIES
D377/AP6D-2
100 Abbott Park Road
Abbott Park, IL 60064-6050
Telephone: (847) 937-9516
Facsimile: (847) 938-2623

Amended Claims

1. (amended) A pharmaceutical composition comprising:

(a)[a] solubilized [HIV protease inhibiting compound] **ritonavir** or a combination of solubilized [HIV protease inhibiting compounds] **ritonavir and another HIV protease inhibiting compound**, or pharmaceutically acceptable salts thereof, **in the amount of from about 1% to about 50% by weight of the total solution**;

(b) a pharmaceutically acceptable organic solvent which comprises a medium and/or long chain fatty acid or a mixture thereof **in the amount of from about 40% to about 75% by weight of the total solution**, and ethanol or propylene glycol **in the amount of from about 1% to about 15% by weight of the total solution**;

(c) water **in the amount of from about 0.4% to about 3.5% by weight of the total solution**; and

(d) optionally, a pharmaceutically acceptable surfactant.

3. (amended) The composition according to Claim 1 **comprising** [wherein said combination of HIV protease inhibiting compounds is 2S,3S,5S)-5-(N-(N-((N-methyl-N-((2-isopropyl-4-thiazolyl)-methyl)amino)carbonyl)-L-valinyl)amino-2-(N-((5-thiazolyl)methoxy-carbonyl)-amino)-1,6-diphenyl-3-hydroxyhexane (ritonavir)] **a combination of ritonavir** and (2S,3S,5S)-2-(2,6-dimethylphenoxyacetyl)-amino-3-hydroxy-5-(2S-(1-tetrahydropyrimid-2-onyl)-3-methyl-butanoyl)amino-1,6-diphenylhexane [(ABT-378)].

4. (amended) The composition according to Claim 1 [wherein said HIV protease inhibiting compound] **comprising ritonavir** or **a** combination of **ritonavir and another** HIV protease inhibiting [compounds is] **compound** selected from the group consisting of:

[(2S,3S,5S)-5-(N-(N-((N-methyl-N-((2-isopropyl-4-thiazolyl)-methyl)amino)carbonyl)-L-valinyl)amino-2-(N-((5-thiazolyl)methoxy-carbonyl)-amino)-1,6-diphenyl-3-hydroxyhexane (ritonavir); 2S,3S,5S)-5-(N-(N-((N-methyl-N-((2-isopropyl-4-thiazolyl)methyl)amino)carbonyl)amino-1,6-diphenyl-3-hydroxyhexane (ritonavir) and]

(2S,3S,5S)-2-(2,6-dimethylphenoxyacetyl)-amino-3-hydroxy-5-(2S-(1-tetrahydropyrimid-2-onyl)-3-methyl-butanoyl)amino-1,6-diphenylhexane;

[N-(2(R)-hydroxy-1 (S)-indanyl)-2(R)-phenylmethyl-4(S)-hydroxy-5-(l-(4-(3-pyridylmethyl)-2(S)-N'-(t-butylcarboxamido)-piperazinyl))-pentaneamide (indinavir)] **indinavir**;

[N-tert-butyl-decahydro-2-[2(R)-hydroxy-4-phenyl-3(S)-[[N-(2-quinolylcarbonyl)-L-asparaginyl]amino]butyl]-(4aS,8aS)-isoquinoline-3(S)-carboxamide (saquinavir)] **saquinavir**;

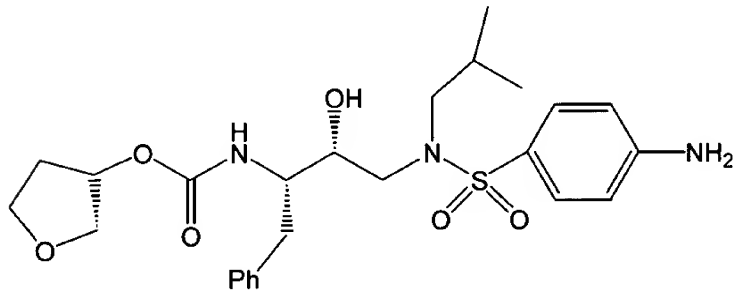
5(S)-Boc-amino-4(S)-hydroxy-6-phenyl-2(R)-phenylmethylhexanoyl-(L)-Val-(L)-Phe-morpholin-4-ylamide;

1 -Naphthoxyacetyl-beta-methylthio-Ala-(2S, 3S)- 3-amino-2-hydroxy-4-butanoyl 1,3-thiazolidine-4-t-butylamide;

5-isoquinolinoxyacetyl-beta-methylthio-Ala-(2S,3S)-3-amino-2-hydroxy-4-butanoyl-1,3-thiazolidine-4-t-butylamide;

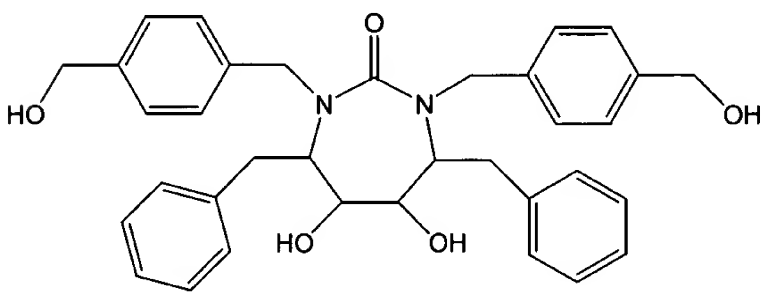
[1S-[1R-(R-),2S*])-N[1] [3-[[[(1,1 -dimethylethyl)amino]carbonyl](2-methylpropyl)amino]-2-hydroxy-1 -(phenylmethyl)propyl]-2-[(2quinolinylcarbonyl)amino]-butanediamide;

[VX-478]



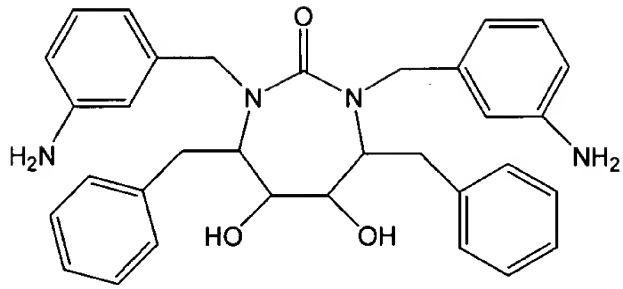
;

[DMP-323]



;

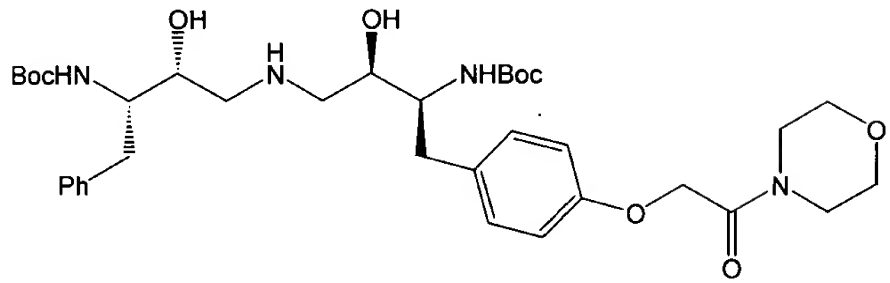
[DMP-450]



;

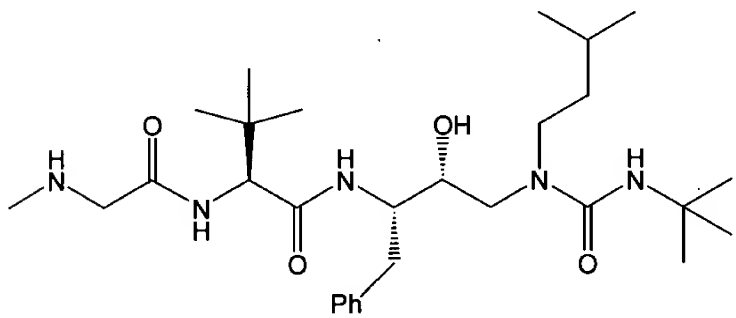
[AG1343 (nelfinavir)] **nelfinavir**;

[BMS 186,318]



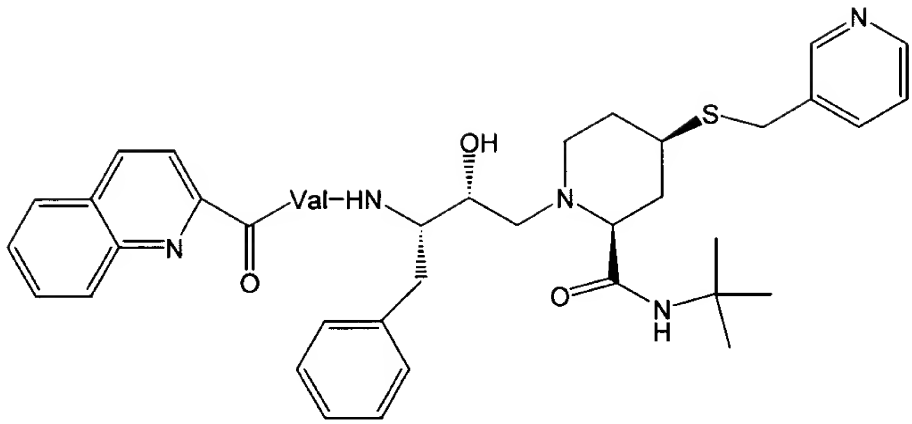
;

[SC-55389a]



;

[BILA 1096 BS]



; and

[U-140690 (tipranavir)] **tipranavir**,
or a pharmaceutically acceptable salt thereof.

5. (amended) The composition according to Claim 1 wherein said [medium and/or long chain] fatty acid is oleic acid.

6. (amended) The composition according to Claim 1 wherein said surfactant is [Polyoxyl] **polyoxyl** 35 castor oil [(Cremophor EL®)].

10. (amended) The composition of Claim 9 [wherein the HIV protease inhibiting compound is] **comprising ritonavir or a combination of ritonavir and another HIV protease inhibiting compound** selected from the group consisting of:
[2S,3S,5S)-5-(N-(N-((N-methyl-N-((2-isopropyl-4-thiazolyl)methyl)amino)carbonyl)amino-1,6-diphenyl-3-hydroxyhexane (ritonavir);
2S,3S,5S)-5-(N-(N-((N-methyl-N-((2-isopropyl-4-thiazolyl)methyl)amino)carbonyl)amino-1,6-diphenyl-3-hydroxyhexane (ritonavir) and (2S, 3S, 5S)-2-(2,6 Dimethylphenoxyacetyl) amino-3-hydroxy-5-[2S-(l-tetrahydro-pyrimid-2-onyl)-3-methyl butanoyl] amino-1,6-diphenylhexane;
N-(2(R)-hydroxy-1 (S)-indanyl)-2(R)-phenylmethyl-4(S)-hydroxy-5-(l-(4-(3-pyridylmethyl)-2(S)-N'-(t-butylcarboxamido)-piperazinyl))-pentaneamide (indinavir)]
(2S, 3S, 5S)-2-(2,6-Dimethylphenoxyacetyl)-amino-3-hydroxy-5-[2S-1-tetrahydro-pyrimid-2-onyl)-3-methyl-butanoyl]-amino-1,6-diphenylhexane;

indinavir;

[N-tert-butyl-decahydro-2-[2(R)-hydroxy-4-phenyl-3(S)-[[N-(2-quinolylcarbonyl)-L-asparaginyl]amino]butyl]-(4aS,8aS)-isoquinoline-3(S)-carboxamide (saquinavir)] **saquinavir**;

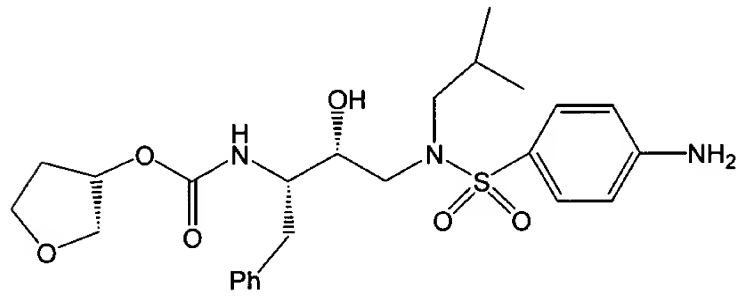
5(S)-Boc-amino-4(S)-hydroxy-6-phenyl-2(R)-phenylmethylhexanoyl-(L)-Val-(L)-Phe-morpholin-4-ylamide;

1 -Naphthoxyacetyl-beta-methylthio-Ala-(2S, 3S)- 3-amino-2-hydroxy-4-butanoyl 1,3-thiazolidine-4-t-butylamide;

5-isoquinolinoxyacetyl-beta-methylthio-Ala-(2S,3S)-3-amino-2-hydroxy-4-butanoyl-1,3-thiazolidine-4 -t-butylamide;

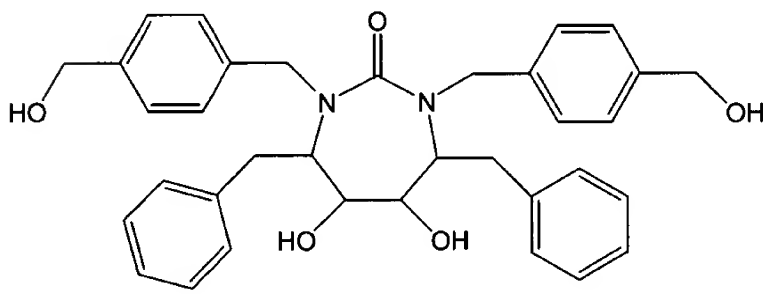
[1S-[1R-(R-),2S*])-N[1] [3-[[[(1,1 -dimethylethyl)amino]carbonyl](2-methylpropyl)amino]-2-hydroxy-1 -(phenylmethyl)propyl]-2-[(2quinolinylcarbonyl)amino]-butanediamide;

[VX-478]



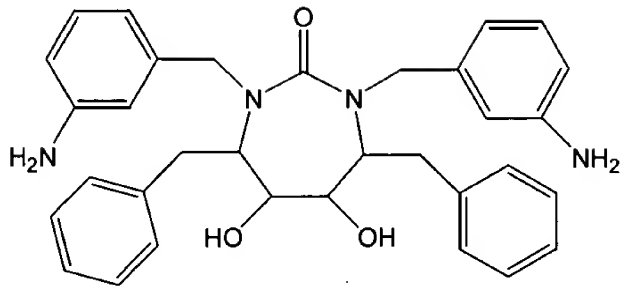
;

[DMP-323]



;

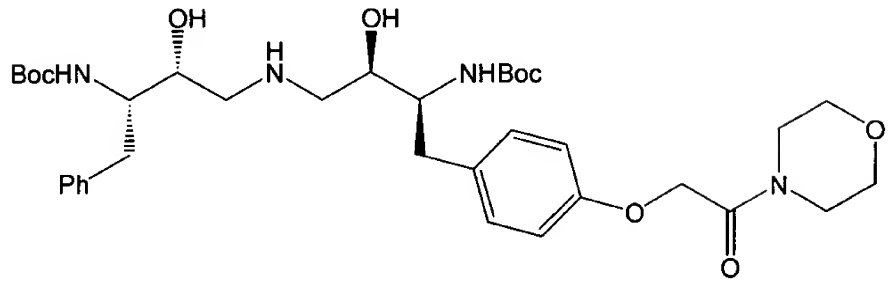
[DMP-450]



;

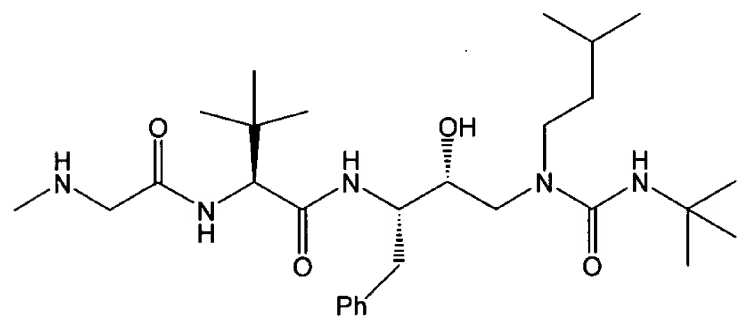
[AG1343 (nelfinavir)] **nelfinavir**;

[BMS 186,318]



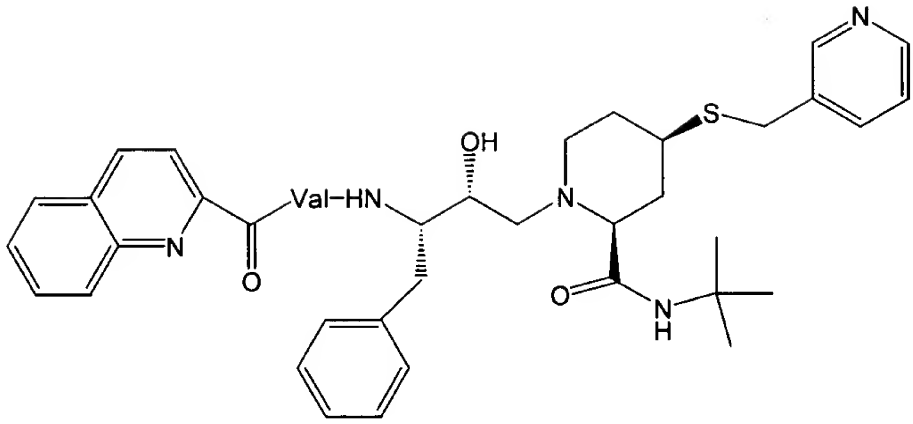
;

[SC-55389a]



;

[BILA 1096 BS]

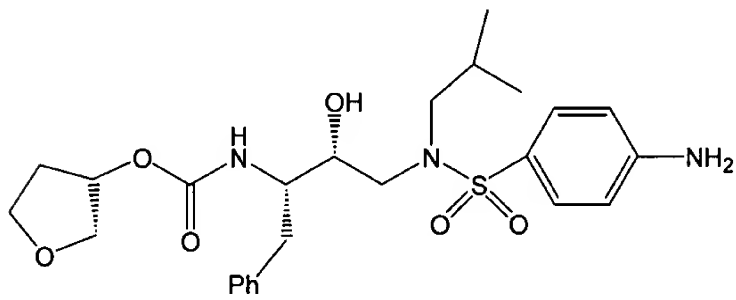


; and

[U-140690 (tipranavir)] **tipranavir**,

or a pharmaceutically acceptable salt thereof.

11. (amended) The composition of Claim 9 [wherein the HIV protease inhibiting compound is ritonavir,] **comprising ritonavir or a combination of ritonavir and another HIV protease inhibiting compound selected from the group consisting of** [(2S, 3S, 5S)-2-(2,6-dimethylphenoxyacetyl) amino-3hydroxy-5-(2S-(l-tetrahydro-pyrimid-2-onyl)-3-methyl butanoyl) amino-1,6diphenylhexane] **(2S, 3S, 5S)-2-(2,6-dimethylphenoxyacetyl) amino-3-hydroxy-5-(2S-(1-tetrahydro-pyrimid-2-onyl)-3-methyl-butanoyl)-amino-1,6-diphenylhexane**, indinavir, saquinavir, nelfinavir, [or VX-478]



---

and tipranavir; or a pharmaceutically acceptable salt thereof.

14. (amended) The composition of Claim 1 which comprises:

(a) ritonavir in the amount of from about 1% to about 30% by weight of the total solution;

(b) a pharmaceutically acceptable organic solvent which comprises (i) oleic acid in the amount of from about [15%] **30%** to about [99%] **75%** by weight of the total solution and (2) ethanol in the amount of from about 3% to about 12% by weight of the total solution; and

(c) water in the amount of from about 0.4% to about [1.5%] **3.5%** by weight of the total solution; and

(d) polyoxyl 35 castor oil in the amount of from about 0% to about 20% by weight of the total solution.

15. (amended) [The composition of Claim 14 which comprises] **A pharmaceutical composition comprising**:

(a) ritonavir in the amount of [from about 5% to] about 10% by weight of the total solution,

(b) a pharmaceutically acceptable organic solvent which comprises (1) oleic acid in the amount of from about 70% to about 75% by weight of the total solution; and (2) ethanol in the amount of from about 3% about 12% by weight of the total solution;

(c) water in the amount of from about 0.4% to about 1.5% by weight of the total solution; and

(d) polyoxyl 35 castor oil in the amount of about 6% by weight of the total solution.

17. The composition of Claim 1 which comprises:

(a) ritonavir and [ABT-378] **(2S, 3S, 5S)-2-(2,6-dimethylphenoxyacetyl)-amino-3-hydroxy-5-(2S-(1-tetrahydro-pyrimid-2-onyl)-3-methyl-butanoyl)-amino-1,6-diphenylhexane** in the amount of from about 1% to about 45% by weight of the total solution;

(b) a pharmaceutically acceptable organic solvent which comprises (i) oleic acid in the amount of from about [15%] **30%** to about [99%] **75%** by weight of the total solution and (2) propylene glycol in the amount of from about 1% to about 15% by weight of the total solution; and

(c) water in the amount of from about 0.4% to about [1.5%] **3.5%** by weight of the total solution.

18. (amended) The composition of Claim 17 which comprises:

(a) ritonavir and [ABT-378] **(2S, 3S, 5S)-2-(2,6-dimethylphenoxyacetyl)-amino-3-hydroxy-5-(2S-(1-tetrahydro-pyrimid-2-onyl)-3-methyl-butanoyl)-amino-1,6-diphenylhexane** in the amount of from about 1% to about 45% by weight of the total solution,

(b) a pharmaceutically acceptable organic solvent which comprises (1) oleic acid in the amount of from about 70% to about 75% by weight of the total solution; and (2) propylene glycol in the amount of from about 1% about 8% by weight of the total solution; [and]

(c) water in the amount of from about 0.4% to about 1.5% by weight of the total solution; **and**

(d) **polyoxyl 35 castor oil in the amount of from about 2.5% to about 10% by weight of the total solution**.